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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/062,831	02/05/2002	Steven M. Ruben	PZ006G13AP1C1D1	1783

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EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/062,831	RUBEN ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,24-36,38-52 and 61-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-15,and 24-36,* is/are allowed.

6)☒ Claim(s) *38,42,61 and 65* is/are rejected.

7)☒ Claim(s) *39-41,43-52,62-64 and 66-74* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 16-23, 37, 53-60, and 75 have been cancelled.

Claims 11, 12, 32, 33, 38, 48, 49, 61, 70, and 71 have been amended.

Claims 1-10, 13, 14, 24-31, 34, and 35 were previously found allowable.

Claims 1-15, 24-36, 38-52, 61-74 are currently pending.

Response to Arguments

The examiner would like to thank applicant for pointing out the clerical error in the previous office action. Applicant has correctly identified that the examiner mistakenly referred to the cDNA HEMCM42 that consists of SEQ ID NO:13, when in reality HEMCM42 is gene 13, with a cDNA sequence of SEQ ID NO:**23** and a polypeptide sequence of SEQ ID NO:59.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. The rejection of claims 11, 12, 22, 23, 32, 33, 48, 49, 59, 60, 70 and 71 under 35 USC 112, second paragraph as being indefinite has been withdrawn due to either the cancellation of the claims in question or amendment of the claims to increase clarity.

3. The rejection of claims 22, 23, 59 and 60 as being incomplete for omitting essential steps has been obviated by the cancellation of these claims.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The rejection of claims 17-23 as not being enabled for the full scope of applicant's claim has been rendered moot by applicant's cancellation of said claims, and as such will not be addressed further.

6. The rejection of claims 17-23 and 53-60 for failing to have adequate written description in the specification as filed has been rendered moot by applicant's cancellation of said claims and will not be addressed further.

7. The rejection of claims 15-23, 36, 37, 52-60, 74, and 75 for lack of enablement for cells that make fragments of antibodies has been withdrawn upon further

consideration, in light of applicant's arguments, and in view of the cancellation of claims 16-23, 37, 53-60 and 75.

8. Applicant's arguments, see pages 13-17, filed December 8, 2004, with respect to the rejection of claims 38-75 as not being enabled have been fully considered and are persuasive. Specifically, Applicant has provided in the response filed December 8, 2004, a statement as to the availability of the biological material deposited as ATCC deposit number 209075. This statement fulfills the requirements of 37 CFR 1.808. Additionally, applicant has argued that it would be routine for one of skill in the art to recover the plasmid containing the cDNA HEMCM42 from the numerous plasmids contained in ATCC deposit number 209075. In light of applicant's arguments and upon further reconsideration, the examiner agrees that it would be a routine matter for one of skill in the art to recover the desired material from ATCC deposit number 209075 given the teachings of the specification and the disclosure of the polynucleotide sequence of HEMCM42. For these reasons the prior rejection of claims 38-75 has been withdrawn.

However, applicant has amended claims 38 and 61. These amendments have necessitated new grounds of rejection as follows:

9. Claims 38, 42, 61, and 65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody that binds SEQ ID NO:59 or a fragment 100% identical to SEQ ID NO:59, does not reasonably provide

enablement for an antibody that binds a sequence 95% identical to SEQ ID NO:59. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant has claimed an antibody that binds to a sequence comprising at least 50 contiguous amino acids that is at least 95% identical to SEQ ID NO:59. The antibodies of the instant invention are disclosed as being useful as immunological probes for the differential identification of tissue of cell types (see particularly page 24, lines 29-31 and page 25, lines 22-24 of the specification). To be used in these applications, the antibodies of the current invention would need to bind the wild type sequence of HEMCM42, that is, SEQ ID NO:59. No working examples of antibodies that bind SEQ ID NO:59 or that bind polypeptides with less that 100% identity to SEQ ID NO:59 appear to be disclosed in the specification. Colman (Research in Immunology, 1994, 145:33-36) teaches that even single amino acid changes can completely disrupt the binding between an antibody and an antigen (see particularly the paragraph that starts in the right column of page 33). As such, it is not clear that an antibody that is specific for a polypeptide that is 95% identical to SEQ ID NO:59 would still bind to the wild type sequence (SEQ ID NO:59). Antibodies that cannot bind this sequence do not appear to be enabled by the specification.

The disclosed use of SEQ ID NO:59 is that it can be used in the treatment or prevention of vascular disorders (see pages 24 and 25 of the specification, particularly page 25, lines 17-22). Applicant's disclosure does not appear to indicate which

residues of SEQ ID NO:59 can be altered while maintaining this use, nor does it appear to clearly define the structure that must be maintained that gives rise to this use.

Skolnick et al. (Trends in Biotechnology, 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see particularly the Abstract and the section titled Sequence-based approaches to function prediction on page 34). Even in situations where there is some confidence of a similar overall structure between two sequences, only experimental research can confirm the artisan's best guess as to the function of the structurally related sequence (see in particular the Abstract and Box 2 on page 36). The complexity of the problem of assigning function based on homology rises as the percent similarity or identity falls (see Whisstock et al., Quarterly reviews of Biophysics, 2003, 36:307-340, particularly the sentence that spans pages 321 and 323).

Given that neither the specification nor the prior art clearly indicate the structural region(s) of the polypeptide of SEQ ID NO:59 that are essential for its role in vascular disorders, and that neither the specification nor the prior art indicate the precise role played by SEQ ID NO:59 in these processes, as skilled artisan would not expect any sequence sharing less that 100% identity with SEQ ID NO:59 to retain the functional properties of SEQ ID NO: 59. The specification does not appear to indicate a separate use for polypeptides 95% identical to SEQ ID NO:59. As such, polypeptide sequences that are 95% identical to SEQ ID NO:59 do not appear to have an enabled use in the specification.

Applicant's claimed genus includes antibodies that bind to polypeptide sequences that are 95% identical to SEQ ID NO:59, yet these polypeptides may not share the structure of SEQ ID NO:59 for the reasons discussed above. Polypeptides that do not share this structure do not appear to be enabled, and therefore the antibodies that bind such polypeptides also lack an enabled use.

In view of the lack of guidance or a working example of an antibody to SEQ ID NO:59 in the specification, the breadth of the claims, and the unpredictability of the prior art, a skilled artisan would not reasonably know how to use an antibody that binds a polypeptide 95% identical to SEQ ID NO:59 since it may not bind the native sequence protein. As such, skilled artisans would not be able to use the antibodies of the claimed invention without undue experimentation.

10. Claims 38, 42, 61, and 65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant has claimed a genus of antibodies that bind SEQ ID NO:59 and sequences that are 95% identical to SEQ ID NO:59. The disclosed use of SEQ ID NO:59 is that it can be used in the treatment or prevention of vascular disorders (see pages 24 and 25 of the specification, particularly page 25, lines 17-22). Applicant's disclosure does not appear to indicate which residues of SEQ ID NO:59 can be altered

while maintaining this use, nor does it appear to clearly define the structure that must be maintained that gives rise to this use.

Skolnick et al. (Trends in Biotechnology, 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see particularly the Abstract and the section titled Sequence-based approaches to function prediction on page 34). Even in situations where there is some confidence of a similar overall structure between two sequences, only experimental research can confirm the artisan's best guess as to the function of the structurally related sequence (see in particular the Abstract and Box 2 on page 36). The complexity of the problem of assigning function based on homology rises as the percent similarity or identity falls (see Whisstock et al., Quarterly reviews of Biophysics, 2003, 36:307-340, particularly the sentence that spans pages 321 and 323).

Given that neither the specification nor the prior art clearly indicate the structural region(s) of the polypeptide of SEQ ID NO:59 that are essential for its role in vascular disorders, and that neither the specification nor the prior art indicate the precise role played by SEQ ID NO:59 in these processes, as skilled artisan would not expect any sequence sharing less that 100% identity with SEQ ID NO:59 to retain the functional properties of SEQ ID NO: 59. Without a definition of the structure that provides for the use of SEQ ID NO:59, it is impossible to describe the structural characteristics of the genus of antibodies that specifically bind polypeptides 95% identical to SEQ ID NO:59 that have the same use. In light of this, one of skill in the art would reasonably conclude

that the disclosure fails to provide a representative number of species to describe the genus of antibodies. Thus, Applicant was not in possession of the claimed genus of all antibodies that bind polypeptides at least about 95% identical to a sequence comprising at least 50 contiguous amino acids of SEQ ID NO:59. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Objections

11. Claims 39-41, 43-52, 62-64, and 66-74 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. Claims 1-15, and 24-36 are allowable since the polypeptide encoded by SEQ ID NO:59 appears to be free of the prior art. A search of the prior art did not uncover antibodies made to the polypeptide of SEQ ID NO:59, or antibodies made to a polypeptide of a sequence different from SEQ ID NO:59 that would cross react with the polypeptide of SEQ ID NO:59 and thus anticipate the instant invention.

13. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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